

Claims

1. Peptide or peptide derivative comprising:
- (a) the amino acid sequence (I)
D-V-N-Y-A-F-L-H-A-T-D-L-L-P-A-C-D-G-E-R,
- (b) the amino acid sequence (II)
S-N-M-Y-A-M-M-I-A-R-F-K-M-F-P-E-V-K-E-K,
- (c) the amino acid sequence (III)
N-W-E-L-A-D-Q-P-Q-N-L-E-E-I-L-M-H-C-Q-T,
- (d) the amino acid sequence (IV)
T-L-K-Y-A-I-K-T-G-H-F-R-Y-F-N-Q-L-S-T-G,
- (e) the amino acid sequence (V)
P-R-Y-F-N-Q-L-S-T-G-L-D-M-V-G-L-A-A-D-W,
- (f) the amino acid sequence (VI)
T-Y-E-I-A-P-V-F-V-L-L-E-Y-V-T-L-K-K-M-R,
- (g) Amino acid sequence (VII)
F-F-R-M-V-I-S-N-P-A-A-T-H-Q-D-I-D-F-L-I,
- (h) partial regions of the amino acid sequence shown in (a), (b), (c), (d), (e), (f) or/and (g) with a length of at least 6 amino acids or/and

RECEIVED
APR 12 1988
CIRCUIT CLERK'S OFFICE

- h 3*
- (i) amino acid sequences which have an essentially equivalent specificity or/and affinity of binding to MHC molecules as the amino acid sequences shown in (a), (b), (c), (d), (e), (f), (g) or/and (h).
2. Peptide or peptide derivative as claimed in claim 1,
wherein
it has at least a length of eight amino acids.
3. Peptide or peptide derivative as claimed in claim 1 or 2,
wherein
it has at least a length of 10 amino acids.
4. Peptide or peptide derivative as claimed in one of the claims 1 to 3,
wherein
it has a length of up to 25 amino acids.
5. Peptide or peptide derivative as claimed in one of the claims 1 to 4
wherein
it carries a marker group.
6. Peptide mimetic,
wherein
it has an essentially equivalent specificity or/and affinity of binding to MHC molecules as a peptide or peptide derivative as claimed in one of the claims 1 to 5.
- an* *SAW C7*

52
X. Complex which at least comprises a peptide or peptide derivative as claimed in one of the claims 1 to 5 or a peptide mimetic as a peptide or peptide derivative as claimed in one of the claims 1 to 5.

7. Complex which at least comprises a peptide or peptide derivative as claimed in one of the claims 1 to 5 or a peptide mimetic as claimed in claim 6 which is bound to a MHC molecule or a peptide-binding derivative of a MHC molecule.
8. Complex as claimed in claim 7,
wherein
it comprises a MHC class II molecule or a peptide-binding derivative thereof.
9. Complex as claimed in claim 8,
wherein
it has a MHC class II molecules of types DR1, DR2, DR4 or DQ6.
10. Complex as claimed in claim 9,
wherein
the MHC class II molecule has the subtype DR B1^{*}101, DR B1^{*}1501, DR B1^{*}1502, DR B1^{*}1601, DR B5^{*}0101, DR B1^{*}0401 or DQ B1^{*}0602.
—
11. Complex as claimed in one of the claims 7 to 10,
wherein
it comprises a recombinant MHC molecule or a peptide-binding derivative thereof.

12. Complex as claimed in claim 11,
wherein
it comprises a soluble peptide-binding derivative
of a MHC molecule.
13. Complex as claimed in one of the claims 7 to 12,
wherein
it carries a marker group.
14. Complex as claimed in one of the claims 7 to 13,
wherein
it at least contains 2 MHC molecules or MHC
molecule derivatives which are associated by
covalent or non-covalent interactions.
15. Complex as claimed in claim 24,
wherein
it contains peptide MHC molecule complexes that are
cross-linked by chemical coupling reagents.
16. Complex as claimed in claim 14,
wherein
it contains MHC molecules or MHC molecule
derivatives that are cross-linked with several MHC-
binding regions via an oligomerized peptide
component.
17. Complex as claimed in claim 14,
wherein
it contains peptide-MHC molecule complexes that are
cross-linked by antibodies.

-445-

- Sut D2*
18. Pharmaceutical composition,
wherein
it contains a peptide or peptide derivative as claimed in one of the claims 1 to 5, a peptide mimetic as claimed in claim 6 or/and a complex as claimed in one of the claims 7 to 17 as the active component if desired in combination with common pharmaceutical additives.
19. Composition as claimed in claim 18,
wherein
it in addition comprises an accessory-stimulating component.
20. Composition as claimed in claim 19,
wherein
the accessory-stimulating component is selected from cytokines or/and the surface antigen B7.
21. Use of a pharmaceutical composition as claimed in one of the claims 18 to 20 for the production of an agent for the diagnosis of diseases or a predisposition for diseases which influence the immune system or for the diagnosis of tumour diseases or a predisposition of tumour diseases.
22. Use as claimed in claim 21 for the production of an agent for the diagnosis of autoimmune diseases or a predisposition of autoimmune diseases.
23. Use as claimed in claim 21 or 22 for the production of an agent for the diagnosis of diabetes or a predisposition of diabetes.

24. Method for the determination of a specific T cell subpopulation,
wherein
a sample containing T cells is contacted with a peptide or peptide derivative as claimed in one of the claims 1 to 5, a peptide mimetic as claimed in claim 6 or/and a complex as claimed in one of the claims 7 to 17 and the reaction of T cells with the peptide or complex is determined in the sample.
25. Method as claimed in claim 24,
wherein
the reaction of the T cells with a fluorescent-labelled peptide or complex is determined by FACS analysis.
26. Method as claimed in claims 24 or 25,
wherein
preactivated T cells are selected before or/and after contacting the T cells with the peptide or the complex.
27. Use of a pharmaceutical composition as claimed in one of the claims 18 to 20 for the production of an agent for therapy or prevention of diseases which influence the immune system.
28. Use as claimed in claim 27 for the production of an agent for the therapy or prevention of autoimmune diseases.
29. Use as claimed in claim 27 or 28 for the production of an agent for the therapy or prevention of diabetes.

30. Use of a peptide or peptide derivative as claimed in one of the claims 1 to 5, a peptide mimetic as claimed in claim 6 or a complex as claimed in one of the claims 7 to 17 for the production of an antigen in particular an immunogen or tolerogen.
31. Method for the isolation of a specific T cell subpopulation,
wherein
a sample containing T cells is contacted with a peptide or peptide derivative as claimed in one of the claims 2 to 5, a peptide mimetic as claimed in claim 6 or a complex as claimed in one of the claims 7 to 17, the T cells that react with the peptide or complex are identified and separated from other T cells if desired.
32. Method as claimed in claim 31,
wherein
preactivated T cells are selected before or/and after contacting the T cells with the peptide or the complex.
33. Use of T cells isolated according to the method as claimed in claim 31 or partial structures thereof for the production of an antigen.
34. Use as claimed in claim 33,
wherein
the T cells or partial structures thereof are re-injected into the patients from whom they are originally derived.

DEPARTMENT OF
PATENTS AND TRADE
MARKS

-47259

35. Use as claimed in claim 34,
wherein
inactivated T cells are reinjected.
36. Use as claimed in claim 35,
wherein
T cells capable of division are reinjected.
37. Antibody against a peptide or peptide derivative as claimed in one of the claims 1 to 5, a peptide mimetic as claimed in claim 6 or a complex as claimed in one of the claims 7 to 17, obtainable by immunization with a peptide, peptide derivative, peptide mimetic or complex and isolating an antibody produced by the immunization.
38. Anti-idiotypic antibody against an antibody as claimed in claim 37, obtainable by immunizing the antibody against the peptide, peptide derivative or peptide mimetic or the complex and isolating an anti-idiotypic antibody produced by the immunization.
39. T cell which reacts with a peptide or peptide derivative as claimed in one of the claims 1 to 3, a peptide mimetic as claimed in claim 6 or a complex as claimed in one of the claims 7 to 17.
40. Use of peptides of glutamic acid decarboxylase (GAD) peptide derivatives derived therefrom or peptide mimetics for the production of a pharmaceutical agent which leads to the formation of an immune tolerance when administered to patients with diabetes.

00000000000000000000000000000000

- 48 -
60
41. Use as claimed in claim 40,
wherein
the peptides, peptide derivatives or peptide mimetics are administered at a dose of 3 to 30 mg per kg body weight.
 42. Use as claimed in claims 40 or 41,
wherein
at least a second vaccination is carried out after administration of the peptides, peptide derivatives or peptide mimetics.
 43. Use as claimed in one of the claims 40 to 42,
wherein
in the second or optionally following vaccinations peptides, peptide derivatives or peptide mimetic complete GAD or/and a part thereof containing the sequence of the peptides which have already been used in the first vaccination are used.
 44. Use as claimed in claim 43,
wherein
the vaccinations are carried out each at intervals of 7 to 14 days.
 45. Use as claimed in one of the claims 40 to 44,
wherein
a mixture of various peptides, peptide derivatives or peptide mimetic is used.

~~-49~~ G1

46. T cell,

wherein

it contains a T cell receptor which binds to a peptide or peptide derivative as claimed in one of the claims 1 to 5, to a peptide mimetic as claimed in claim 6 or to a complex as claimed in one of the claims 7 to 17.

47. T cell as claimed in claim 46,

wherein

it has a T cell receptor which comprises a TCR α chain containing a CDR3 region shown in fig. 5 or one that is at least 70 % homologous thereto or/and a TCR β chain containing a CDR3 region shown in fig. 6 or one that is at least 70 % homologous thereto.

48. Polypeptide with T cell receptor activity,

wherein

it binds to a peptide or peptide derivative as claimed in one of the claims 1 to 5, to a peptide mimetic as claimed in claim 6 or to a complex as claimed in one of the claims 7 to 17.

49. Polypeptide as claimed in claim 48,

wherein

it comprises a TCR α chain containing a CDR3 region shown in fig. 5 or an amino acid sequence that is at least 70 % homologous thereto.

50. Polypeptide as claimed in claim 48 or 49,

wherein

it comprises a TCR β chain containing a CDR3 region shown in fig. 6 or an amino acid sequence that is at least 70 % homologous thereto.

DRAFTED BY: GAGGOGO

- 50 - 62

51. Nucleic acid,
wherein
it codes for a polypeptide as claimed in one of the
claims 48 to 50.

(Add) 3

Add
gt } 4